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(54) Device and method for separating components of a fluid sample

(57) A device and method is provided for separating heavier and lighter fractions of a fluid sample. The device includes a collection tube, a flowable liquid separation medium and a deformable container. A separation medium is contained within the deformable container and the deformable container is positioned within the collection tube and is deformably reconfigurable under centrifugation from a first condition permitting liquid collection within the tube to a second condition establishing physical separation between the separated liquid phases.

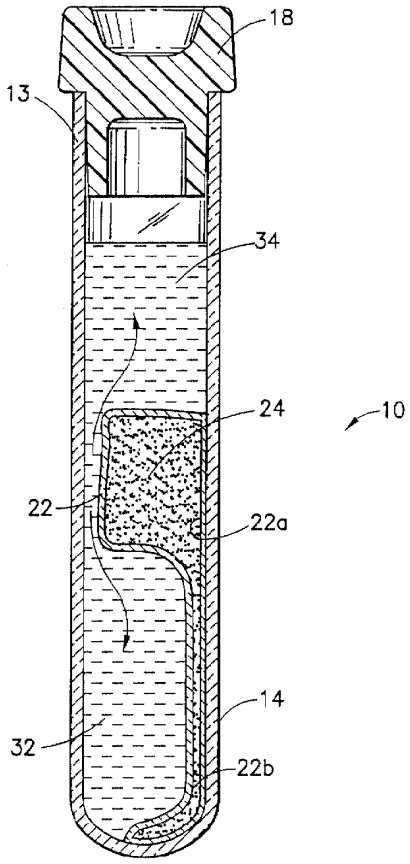

FIG.4

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Description

BACKGROUND OF THE INVENTION

1. Field of the Invention

[0001] This invention relates to a device and method for separating heavier and lighter fractions of a fluid sample. More particularly, this invention relates to a device and method for collecting and transporting fluid samples whereby the device and fluid sample are subjected to centrifugation in order to cause separation of the heavier fraction from the lighter fraction of the fluid sample.

2. Description of Related Art

[0002] Diagnostic tests may require separation of a patient's whole blood sample into components, such as serum or plasma, the lighter phase component, and blood cells, the heavier phase component. Samples of whole blood are typically collected by venipuncture through a cannula or needle attached to a syringe or an evacuated collection tube. Separation of the blood into serum and blood cells is then accomplished by rotation of the syringe or tube in a centrifuge. Such arrangements use a barrier for moving into an area adjacent the two phases of the sample being separated in order to maintain the components separated for subsequent examination of the individual components.

[0003] A variety of devices have been used in collection and separation devices to divide the heavier and lighter phases of a fluid sample.

[0004] The most widely used device includes thixotropic gel material such as polyester or silicone gels. The present gel serum separation tubes require special manufacturing equipment to prepare the gel and to fill the tubes. Moreover, the shelf-life of the product is limited in that over time unbound resin may be released from the gel mass. This resin may have a specific gravity that is less than or equal to the separated serum and may float in the serum and may clog the measuring instruments such as the instrument probes used during the clinical examination of the sample collected in the tube. Such clogging can lead to considerable downtime for the instrument to remove the clog.

[0005] In addition, no commercially available gel is completely chemically inert to all analytes. If certain drugs are present in a blood sample when it is taken, there can be a chemical reaction at the gel interface.

[0006] Therefore, a need exists for a separator device that (i) is easily used to separate a blood sample; (ii) is independent of temperature during storage and shipping; (iii) is stable with radiation sterilization; (iv) employs the benefits of a thixotropic gel barrier yet avoids the many disadvantages of placing a gel in contact with the separated blood components; (v) minimizes cross contamination of the heavier and lighter phases of the sample; (vi) minimizes entrapment of the lower and higher density materials within the separator device; (vii) is able to move into position to form a barrier in less time than conventional methods and devices; (viii) is able to provide a clearer serum or plasma specimen with less cell contamination than conventional methods and devices; and (ix) can be used with standard sampling equipment.

SUMMARY OF THE INVENTION

[0007] The present invention is a method and assembly for separating a fluid sample into a higher specific gravity phase and a lower specific gravity phase. Desirably, the assembly of the present invention comprises a plurality of constituents. Preferably, the assembly comprises a container, such as a tube, a deformable container, such as a bag, and a flowable separation medium.

[0008] Most preferably, the deformable container is provided for positioning within a tube and includes a flowable fluid separation medium capable of maintaining separation of the separated fluid phases. The deformable container is deformably repositionable under centrifugation from a first condition permitting a fluid sample within the tube to a second condition establishing a physical separation between the separated fluid phases.

[0009] Preferably, the deformable container includes a flexible bag which is reconfigurable under centrifugation from a first condition to a second condition. The flowable fluid separation medium preferably includes a thixotropic fluid such as a gel having a specific gravity, which under centrifugation, becomes resident between the separated fluid sample phases. The flexible bag may be adheringly secured to the inner wall of the tube so as to provide for the deformable movement of the bag and the gel contained therein from a position adjacent the lower end of the tube to an intermediate position within the tube under centrifugation so as to establish residence of the gel in the bag between the separated fluid phases of the fluid sample. The flexible bag is preferably sealed with the gel completely contained therein.

[0010] The assembly of the present invention is advantageous over existing separation products that use gel. One advantage is that the assembly of the present invention will not interfere with analytes as compared to gels that may interfere with analytes. In particular, the assembly will not interfere with therapeutic drug monitoring analytes.

[0011] Another notable advantage of the present invention is that fluid specimens are not subjected to low density residuals such as unbound resins that are at times available in products that use gel.

[0012] Additionally, the assembly of the present invention does not require any additional steps or treatment by a medical practitioner whereby a blood or fluid sample is drawn in the conventional way, using standard

sampling equipment.

DESCRIPTION OF THE DRAWINGS

[0013] FIG. 1 is a perspective view of the assembly of the present invention including a gel-containing flexible bag supported within a tube.

[0014] FIG. 2 is a longitudinal sectional view of the device of FIG. 1 taken along line 2-2 thereof.

[0015] FIG. 3 is a longitudinal sectional view of the assembly of FIG. 1 taken along line 2-2 thereof illustrating fluid delivery into the assembly by a needle.

[0016] FIG. 4 illustrates the assembly under centrifugation and the movement of the separating means.

[0017] FIG. 5 illustrates the assembly after centrifugation and the separation of the fluid sample into higher and lower specific gravities.

[0018] FIG. 6 is a perspective view of the unassembled elements of an alternative embodiment of the assembly of the present invention.

[0019] FIG. 7 is an exploded perspective view of a further embodiment of the present invention.

[0020] FIGS. 8A-8D show, in partial section, further embodiments of a tube used in accordance with the assembly of the present invention.

DETAILED DESCRIPTION

[0021] The present invention may be embodied in other specific forms and is not limited to any specific embodiments described in detail, which are merely exemplary. Various other modifications will be apparent to and readily made by those skilled in the art without departing from the scope and spirit of the invention. The scope of the invention will be measured by the appended claims and their equivalents.

[0022] Referring to FIGS. 1 and 2, assembly **10** of the present invention is shown. Assembly **10** includes a collection tube **12** having an upper end **13**, a lower end **14** and a cylindrical wall **15** extending therebetween. The upper end **13** includes an opening **13a**, while lower end **14** is closed by an integrally formed bottom **14a.** A tube interior **16** is defined between upper and lower ends **13** and **14.** Opening **13a** of upper end **13** of tube **12** may be closed by a stopper **18** which is made of a suitable elastomer material. Alternatively, both ends of the tube may be open and both ends of the tube may be sealed by elastomeric closures. At least one of the closures of the tube may include a resealable septum.

[0023] Supported within tube **12** is a fluid phase partition device **20**. Fluid phase partition device **20** includes a deformable container or flexible bag **22** and a thixotropic separation medium or a Gel **24** contained within bag **22**.

[0024] Bag **22** may be a flexible deformable bag which is subject to being reconfigured upon an application of force. Bag **22** may be formed from a wide variety of both elastic and inelastic materials such as polyethylene, polyurethane or syran and which does not adversely interact with the fluid sample which would come in contact with the bag. The size of the bag is selected such that if the bag were to be completely or partially expanded it would have a dimension which would exceed the diameter of tube **12**. Bag **22** is thus expandable into a configuration where it may be placed in frictional engagement with the inner surface **15a** of cylindrical wall **15** of tube **12.** Bag **22** while being deformably flexible and pliable has sufficient strength so as to permit bag deformation without risk of rupturing of the bag. Bag **22** may be formed with conventional forming techniques such as film extrusion or blow molding.

[0025] As shown in FIGS. 1 and 2, bag **22** contains a gel **24** in sealed containment therein. Gel **24** is selected so that it becomes resident between the separated phases of a fluid sample. Most preferably, gel **24** is selected to have a specific gravity intermediate the specific gravities of the lighter serum or plasma phase and the heavier cellular phase of a blood sample.

[0026] When subjected to forces such as centrifugal forces, gel **24** becomes flowable. Upon cessation of such centrifugal forces, gel **24** may return to its non-flowable state.

[0027] Gel **24** of the present invention may be a single component gel or may formed of various combinations of gels and fluids. Gel **24** may include silicones or oils or mixtures thereof such as mixtures of silicon and hydrophobic silicon dioxide powders or a mixture of liquid polybutane polymer and silicon dioxide powder. While these specific examples are provided, gel **24** can be of any material which is movable under centrifugal force to form a barrier between the separated blood phases of a blood sample. In an alternative embodiment, a highly viscous material, rather than a gel, may be used.

[0028] As shown in FIGS. 1 and 2, gel **24** fills only a portion **22b** of bag **22** with the remaining portion **22a** of the bag being collapsed and substantially absent of gel.

[0029] Bag **22** is inserted into tube **12** and positioned in lower end **14** of tube **12**. Bag **22** may be secured adjacent bottom **14a** oftube **12** by using a suitable adhesive. Adhesive may be applied between bag **22** and inner surface **15a** of cylindrical side wall **15** of tube **12** adjacent bottom **14a.** It is contemplated that bag **22** may also be secured to inner surface **15a** at one or more locations along the length of tube **12**. While an applied adhesive may be used to secure bag **22** to inner surface **15a** of tube **12,** it is contemplated that the bag itselfmay be formed of materials which have sufficient tackiness to promote adherence of bag **22** to inner surface **15a** of tube **12.** In an alternative embodiment, the flexible bag is not attached within the tube but is free to move with the gel.

[0030] As shown in FIGS. 3-5, liquid sample **30** is delivered into interior **16** of a collection tube **12** by a needle **19** that pierces through elastomeric stopper **18** and then the needle is removed and the stopper reseals. For purposes of illustration only, the liquid sample is blood. Liq-

uid sample **30** substantially fills interior **16** of tube **12** between bag **22** and upper end **13** of tube **12**. Tube **12** is then placed in a centrifuge device such that closed lower end **14** will be positioned radially outward of stopper **18** and the axis of rotation of the centrifuge during centrifugation. During centrifugation blood cells and other components of the heavy or higher density cellular phase **32** move toward closed lower end **14** of tube **12**. The lighter or lower density phase components such as plasma or serum move toward open end **13**. As shown in FIG. 4, gel **24** moves within bag **22** from a position adjacent the closed lower end **14** of tube **12** towards upper end **13** to reside at a position intermediate opposed upper and lower ends **13** and **14**. Serum or plasma is squeezed upwardly and cells are squeezed downwardly at the interface. Bag **22** forms a physical separation between the separated phases.

[0031] As shown in FIG. 5, after centrifugation, lower portion **22b** of bag **22** collapses while upper portion **22a** of bag **22** that is filled with gel **24** provides separation between the lighter phase blood components **34** such as plasma or serum and the heavier phase cellular blood components **32**.

[0032] As shown in FIG. 6, an alternative embodiment of the present invention is illustrated. Bag **42** is substantially similar to bag **22** described above with a portion of its maximum volume filled with Gel **44** of the type described above. However, in the alternative embodiment bag **42** is inserted into interior **16** of tube **12** and is not adhesively retained in the lower end. Thus, upon centrifugation, the bag deformably reconfigures to move from a position adjacent lower end **14** of tube **12** to a more intermediate position along the tube to thereby provide the physical barrier between the centrifuged blood phases. The gel-filled bag is deformably and partially collapsed so as to permit blood phase separation during centrifugation.

[0033] As shown in FIG. 7, an alternative embodiment of the present invention is illustrated. The alternate embodiment is a flexible bag **52** having a central passageway **53** therethrough. Bag **52** is filled with a gel and has a passageway **53** for passage of blood therethrough. Bag **52** is placed within interior **16** of tube **12** and may be located at a final intermediate location within tube **12** between upper end **13** and lower end **14** and may be adheringly supported to the side wall. Blood is delivered through central passageway **53** and into tube **12**. Upon centrifugation, the blood components may flow through passageway **53** and be separated into the heavier and lighter phases. Centrifugation causes the bag to collapse inwardly around passageway **53** closing the passageway and establishing a physical barrier between the separated blood phases.

[0034] As shown in FIGS. 8A-D, in order to maintain the relative positioning of the gel-containing bag after centrifugation between the separated blood phases, cylindrical wall **15** of tube **12** may be modified to promote bag retention.

[0035] As shown in FIG. 8A, the tube **12'** may include cylindrical wall **15'** having a plurality of annular inwardly directed projections or ribs **17'** which are spaced apart along the length of tube **12'**. These ribs **17'** provide a frictional surface for retentatively supporting the gel-containing bag as it moves between the blood phases during centrifugation. Ribs **17'** are positioned along tube **12'** at an area **21'** which most closely approximates the location where blood phase separation may occur.

[0036] As shown in FIG. 8B, tube **12"** includes a plurality of annular recesses **17"** which are similar to ribs **17'**. Recesses **17"** support the gel containing bag during centrifugation.

[0037] Other examples of shapes and configurations of spaced apart annular ribs are shown in FIGS. 8C and 8D. These shapes may be continuously along the circumference as shown or they may be intermittently located at areas around the circumference.

[0038] The present invention may be further modified to provide additional benefits in blood collection and testing. The present invention contemplates that the bag used to contain the gel could be coated with a clot activator to enhance clotting of a blood sample. Furthermore, these clot activators may include a surfactant such as a silicone and/or polyvinylpryolidine. The bag could also be coated with other blood interacting materials as may be desired for particular tests. These materials include heparin or protamine sulfates. Further the bag may be coated with an agglutinizing agent to promote inter-cellular adhesion for fast and efficient separation.

[0039] An alternative embodiment of the present invention includes a rigid member that is contained or attached to a flexible bag. Preferably, the rigid member is in the form of an elongated rod which is in the direction of gel flow. The rod serves to help the flexible bag erect. When inside the bag, the rod also eases gel flow by means of capillary action.

Claims

1. A collection device for maintaining separation between liquid phases separated by centrifugation or the like comprising:

   an elongate collection tube for accommodating collected liquid;

   a flowable liquid separation medium capable of maintaining separation of said separated liquid phases; and

   a deformable container for retaining said liquid separation medium, said container being positioned within said collection tube and being deformably repositionable with said centrifugation from a first condition permitting said liquid col-

lection within said tube to a second condition establishing physical separation between said separated liquid phases.

2. The collection device of Claim 1, wherein said deformable container is a flexible bag.

3. The collection device of Claim 2, wherein said flexible bag is deformably reconfigurable under said centrifugation from said first condition to said second condition.

4. The collection device of Claim 3, wherein said tube is an elongate cylindrical member having an open end, a closed end, and a generally cylindrical wall therebetween.

5. The collection device of Claim 4, wherein said bag is captively retained within said tube.

6. The collection device of Claim 5, wherein said bag is secured to said cylindrical wall of said tube and is deformable from said first condition wherein said medium within said bag is located at said closed end of the tube, to said second condition wherein said medium within said bag is located at an intermediate position between said open and closed ends.

7. The collection device of Claim 4, wherein said bag is secured to said wall along at least one location.

8. The collection device of Claim 4, wherein said bag is secured to said wall with an adhesive.

9. The collection device of Claim 2, wherein said bag is formed from materials selected from the group consisting of polyethylene, polyurethane, polyvinyl chloride, polyester, polyolefin, polyether or combinations thereof.

10. The collection device of Claim 2, wherein said bag includes a clot enhancing substance for contact with said collected liquid.

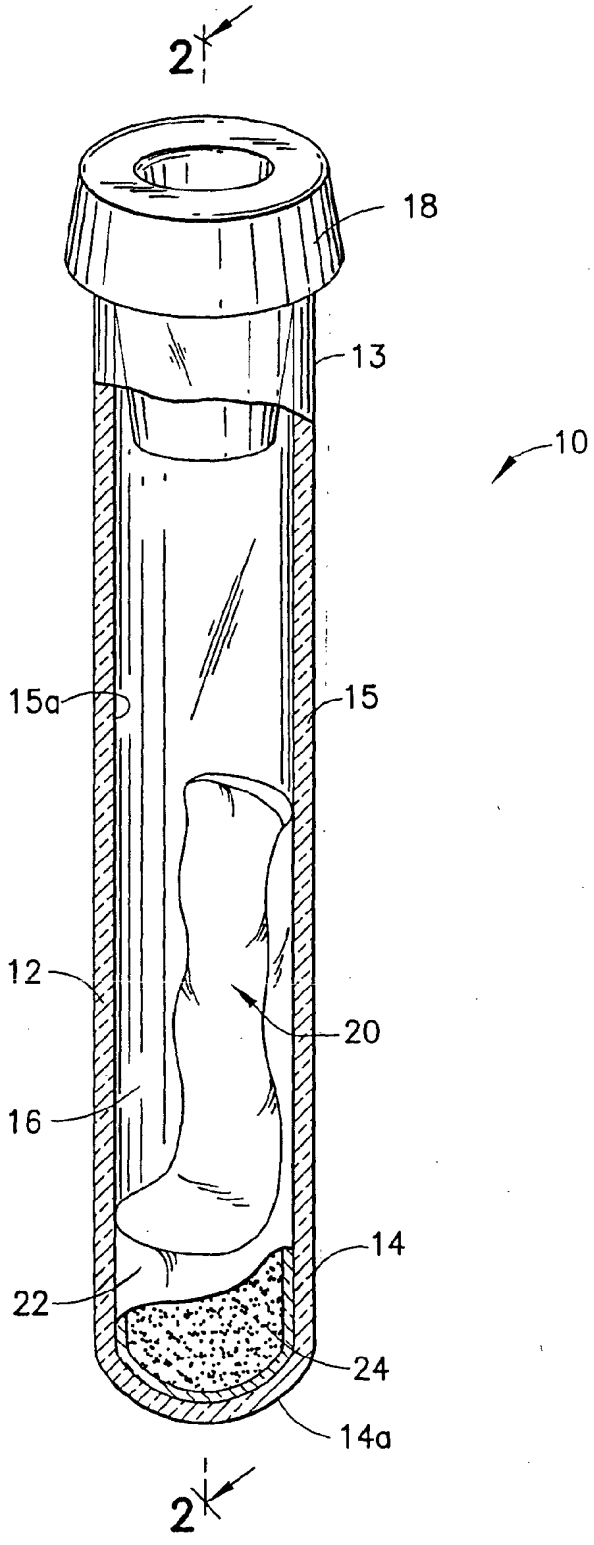

FIG. 1

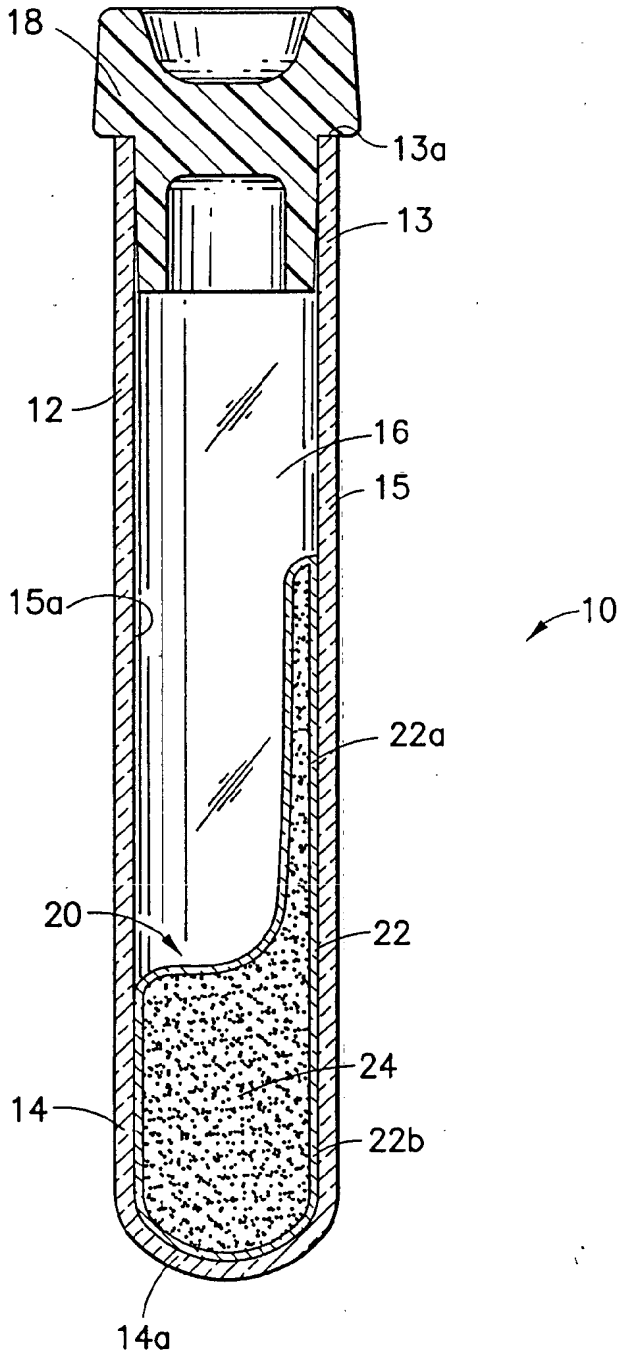

FIG.2

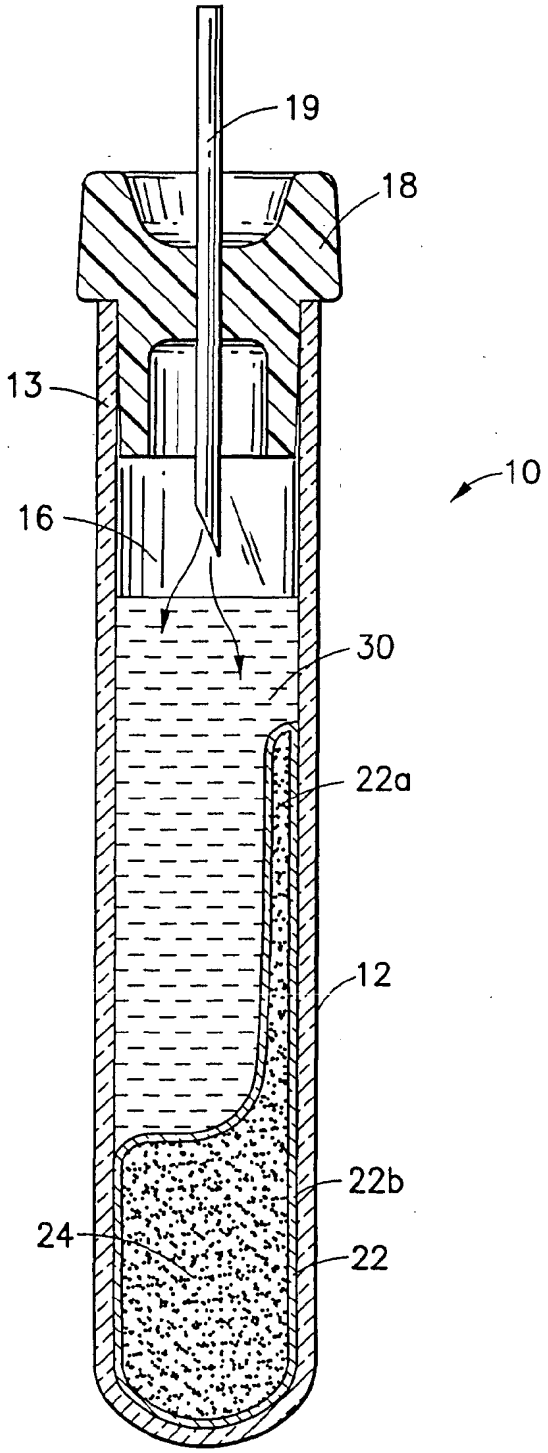

FIG.3

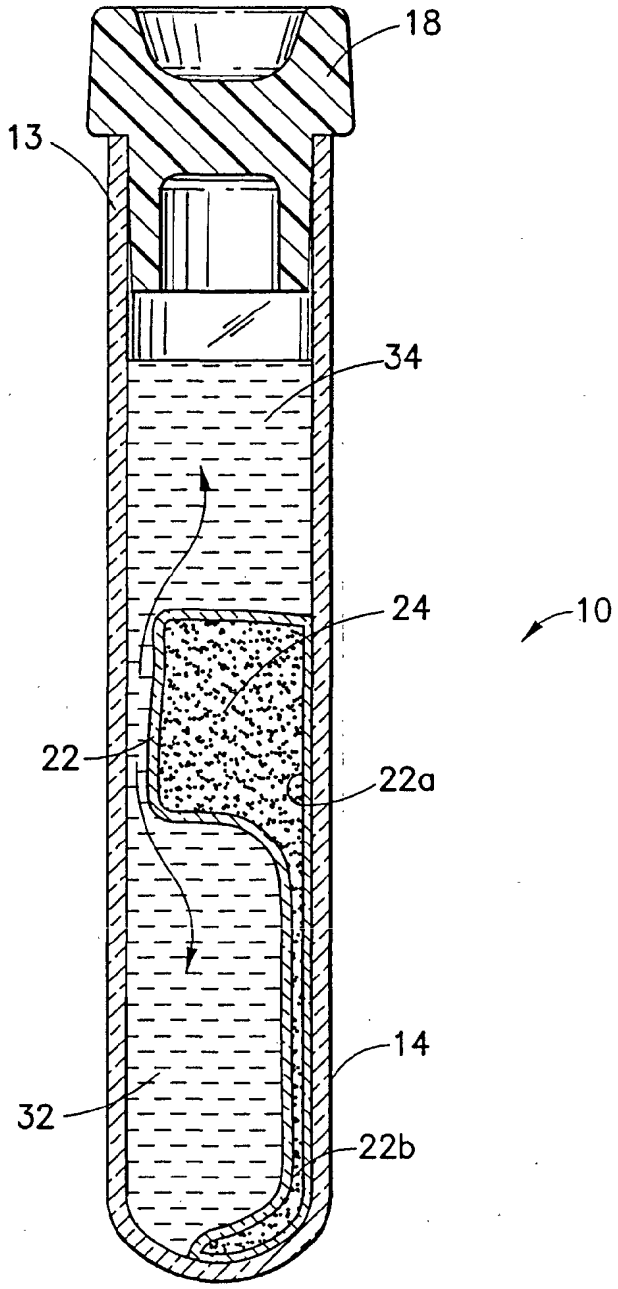

FIG.4

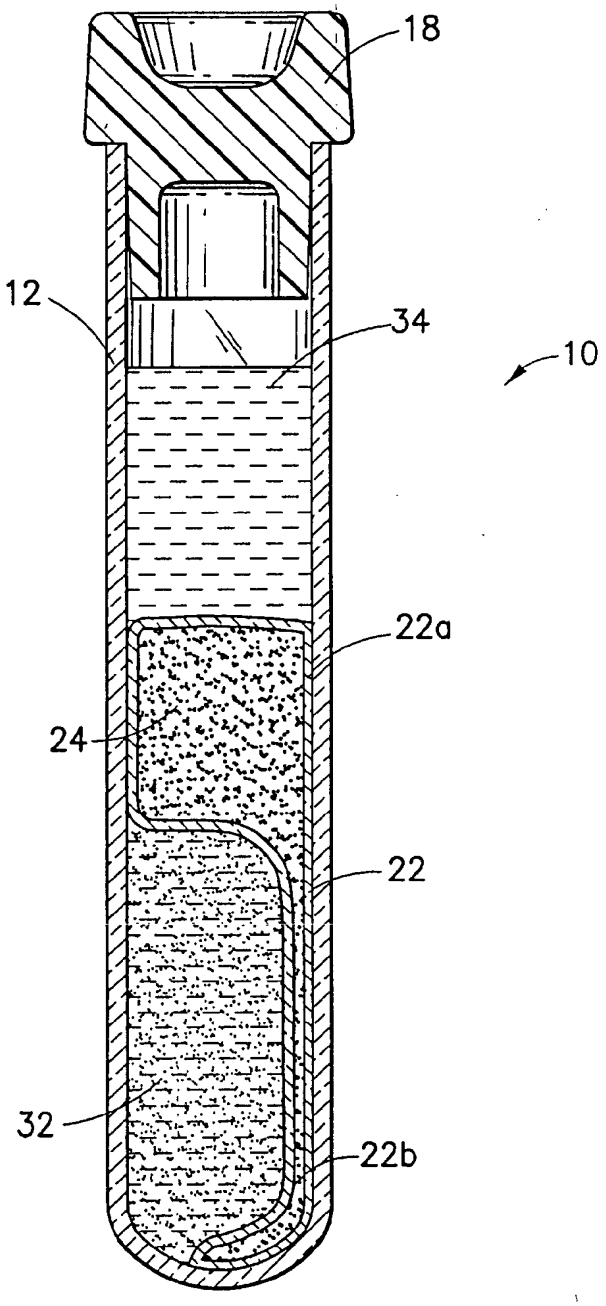

FIG.5

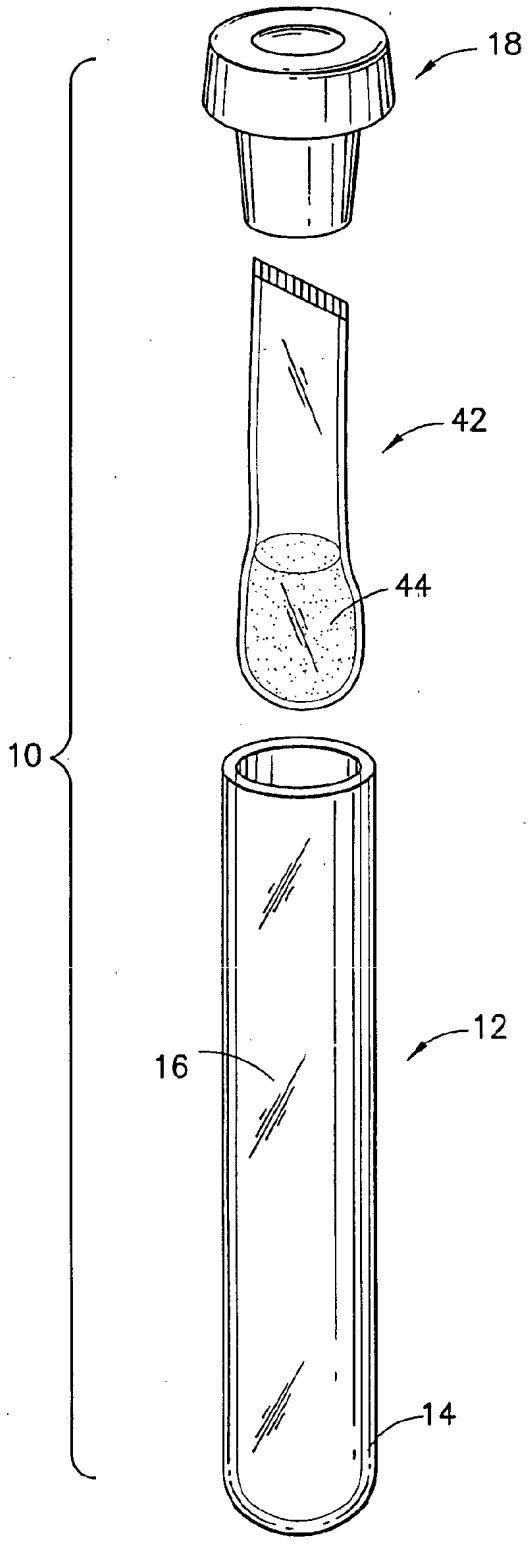

FIG.6

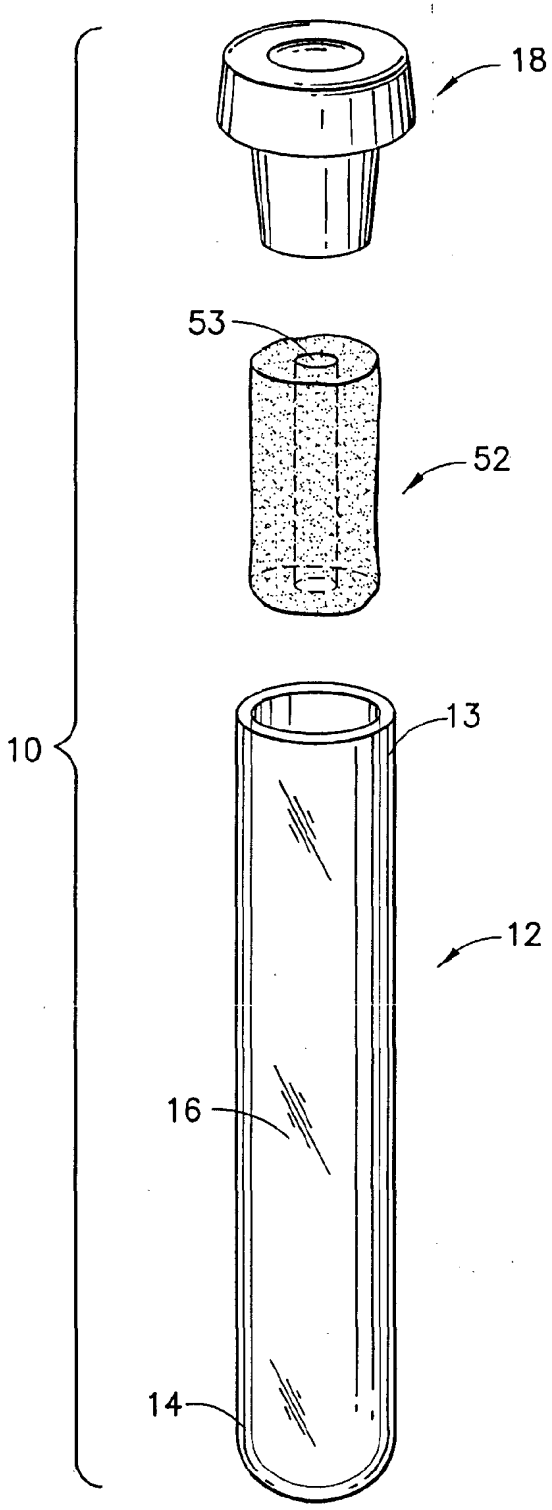

FIG.7

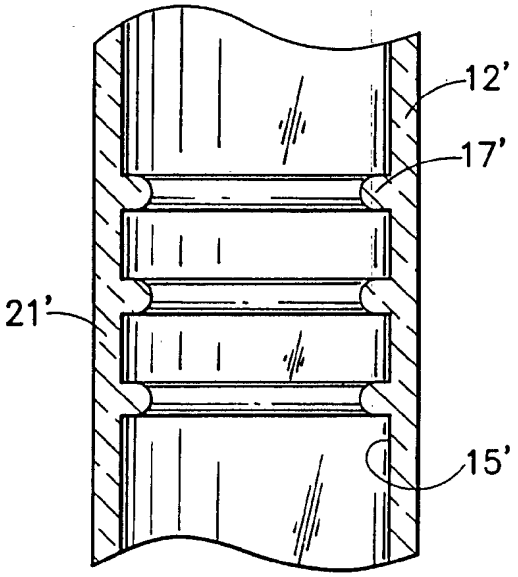

FIG.8A

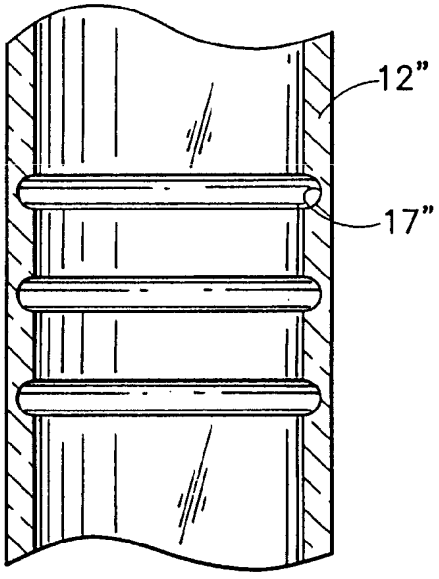

FIG.8B

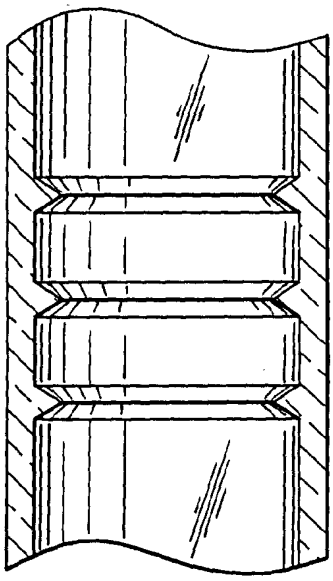

FIG.8C

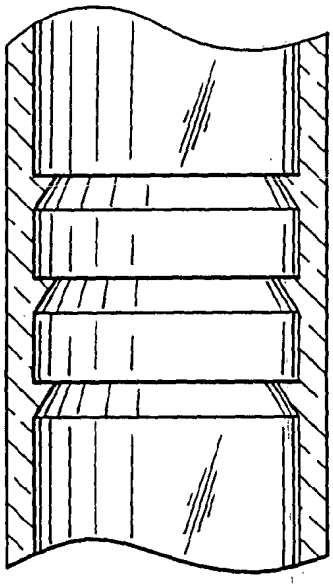

FIG.8D